## REMARKS

This paper is being filed in response to the Office Action dated January 15, 2002. Applicants respectfully request reconsideration of the above-identified application in light of the amendments and remarks presented in the instant Response.

Claims 1-11 are pending. Claims 2, 4, and 5 have been cancelled. Claims 1, 3, 8, 9, and 10 have been amended. New claim 15 has been added. Amendments to the specification paragraphs correct typographical errors and are fully supported by the application as filed. For example, the specification as originally filed discloses:

> The human LYC3 protein has a signal peptide of 18 amino acids (residues 1-18 of SEQ ID NO: 4). After cleavage of the signal peptide, the mature human LYC3 protein has the amino acid sequence of residues 19-146 of SEQ ID NO: 4. Example 2 at page 8, lines 21-23

Therefore, amendments to the specification do not constitute new matter. Amendments to the claims are fully supported by the specification as originally filed and, therefore, do not constitute new matter. New claim 15 is supported, *inter alia*, by original claims 4 and 5.

**Claims Share a Special Technical Feature**

The Examiner has alleged that Claims 4 and 5 do not share a special technical feature with claims 1-3 and 6-11 in view of de Baetselier. Applicants have provisionally elected claims 1-3 and 6-11 and have cancelled claims 4 and 5. Applicants reaffirm this election, but respectfully request reconsideration of the restriction requirement in view of new claim 15 and the amendments made herein to the original claims. Applicants assert that the amended claims are not anticipated or obvious in view of de Baetselier and, therefore, share a special technical feature.

**Claims Are Drawn to Patentable Subject Matter**

Claims 1-3 and 6-11 have been rejected under 35 U.S.C. §101 as allegedly unsupported by a credible asserted or well established utility. The Examiner has alleged that the specification does not disclose a specific function of the protein of SEQ ID NO:4 or its relationship to any disease. The Examiner has alleged further that identification of the protein of SEQ ID NO:4 as a lysozyme is only based on homology to known lysozymes.

Applicants traverse this rejection and assert that the claims are drawn to patentable subject matter. Applicants respectfully invite the Examiner's attention to Example 6 of the application. This example clearly demonstrates that a polypeptide having the amino acid sequence of SEQ ID NO:4 has bacteriolytic activity. Therefore, Applicants have established that LYC3 may be used in any of the well established applications of antimicrobial agents.

Applicants do not concede, however, that the utility of LYC3 is limited to that of an antimicrobial agent. Applicants respectfully invite the Examiner's attention to the Revised Interim Utility Guidelines:

> A patent examiner must accept a utility asserted by an applicant unless the Office has evidence or sound scientific reasoning to rebut the assertion. The examiner's decision must be supported by a preponderance of all the evidence of record. *In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). More specifically, when a patent application claiming a nucleic acid asserts a specific, substantial, and credible utility, and bases the assertion upon homology to existing nucleic acids or proteins having an accepted utility, the asserted utility must be accepted by the examiner unless the Office has sufficient evidence or sound scientific reasoning to rebut such an assertion. "[A] 'rigorous correlation' need not be shown in order to establish practical utility; 'reasonable correlation' is sufficient." *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1565, 39 USPQ2d 1895, 1900 (Fed. Cir. 1996). The Office will take into account both the nature and degree of the homology. 66 Fed. Reg. 1092, 1096 (Janyary 5, 2001)(emphasis added).

Applicants assert that LYC3 has utility in any of the applications for lysozyme recited in the specification, *inter alia*, page 6, lines 18-23 and 30-36, or known to those of ordinary skill in the

art. This assertion is based in part on the homology of LYC3 to known lysozymes as well as on the demonstrated bacteriolytic activity. Applicants believe that since the Examiner's allegations contravene neither Applicant's clear data showing bacteriolytic activity nor Applicant's assertions of other utility, the Examiner has failed to show "by a preponderance of all the evidence of record" that Applicant's invention lacks utility. *Id.* Applicants, therefore, respectfully request withdrawal of this rejection.

**Claims Are Fully Enabled**

Claims 1-3 and 6-11 have been rejected under 35 U.S.C §112, first paragraph as allegedly non-enabled. Applicants traverse this rejection and assert that the amended claims are fully enabled by the disclosure. The instant claimed invention conveys to one of ordinary skill in the art the utility of the LYC3, *inter alia*, as a bacteriolytic agent, a pharmaceutical, and an anti-tumor agent, in sufficient detail as to require nothing more than reasonable experimentation to practice the full scope of the claims.

**Claims Are Fully Described**

Claims 1-3 and 6-11 have been rejected as allegedly drawn to subject matter that was not described in the specification as to reasonably convey to one skilled in the art that the inventors had possession of the invention. Applicants traverse this rejection and assert that the amended claims are drawn to subject matter clearly described in the specification and of which Applicants had possession at the time the application was filed.

**Claims Are Clear and Definite**

Claims 1-3 and 6-11 have been rejected under 35 U.S.C §112, second paragraph as allegedly vague and indefinite. Applicants traverse this rejection and assert that the amended claims are clear and definite.

**Claims Are Novel**

Claims 1-3 and 6-11 have been rejected under 35 U.S.C §102(b) as allegedly anticipated by Jung et al. (Accession V00428)(hereinafter "Jung"). The Examiner has alleged that claim 2 is not patentable over the sequence of Jung since the Jung sequence will allegedly hybridize to nucleotides 81-521 of SEQ ID NO:3.

Applicants traverse this rejection and assert that Jung does not anticipate the amended claims. The sequence of Jung fails to teach every element of the claimed invention because it does not encode a polypeptide having the amino acid sequence of SEQ ID NO:4 nor amino acids 19-146 of SEQ ID NO:4 as illustrated on the attached sheet captioned "Alignment." The translation products of all three reading frames of the Jung sequence are shown. A multiple sequence alignment was performed with these polypeptides and SEQ ID NO:4 of the instant invention. Applicants invite the Examiner's attention to the substantial differences in the amino acid sequence of these polypeptides. *See* Alignment. Applicants, therefore, respectfully request withdrawl of this rejection.

For the foregoing reasons, Applicants believe that the amended claims are in condition for allowance and respectfully request prompt issuance of a Notice of Allowance.

Applicants believe that no fees are due with this response. Any required fees may be charged to Deposit Account No. 02-4377. Two copies of this sheet are enclosed.

Respectfully submitted,

April 15, 2002

Rochelle K. Seide
PTO Reg. No. 32,300

Attorney for Applicant
BAKER BOTTS, L.L.P.
30 Rockefeller Plaza
New York, NY 10112
(212) 408-2626

Enclosures

## VERSION WITH MARKINGS TO SHOW CHANGES MADE

This marked-up version was prepared with DeltaView software (v2.5.163). In this section, added text is marked with double underlining. *e.g.* added text, and deleted text is marked by a single strikethrough, *e.g.* ~~deleted text~~.

IN THE SPECIFICATION

The paragraph beginning on page 1, line 36 and ending on page 2, line 3 has been **amended** as follows:

In one aspect, the invention provides an isolated DNA molecule, which comprises a nucleotide sequence encoding a polypeptide having human LYC3 protein activity, wherein said nucleotide sequence shares at least 70% homology to the nucleotide sequence of nucleotides 81-521 in SEQ ID NO: 3, or said nucleotide sequence can hybridize to the nucleotide sequence of nucleotides 81-521 in SEQ ID NO: 3 under moderate stringency. Preferably, said nucleotide sequence encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 4 or of ~~20-148~~amino acids 19-146 ~~in~~of SEQ ID NO: 4. More preferably, the sequence comprises the nucleotide sequence of nucleotides 81-521 in SEQ ID NO: 3.

The paragraph beginning on page 2, line 4 and ending on page 2, line 7 has been **amended** as follows:

Further, the invention provides an isolated LYC3 polypeptide, which comprises a polypeptide having the amino acid sequence of SEQ ID NO: 4 or of ~~20-148~~amino acids 19-146 ~~in~~of SEQ ID NO: 4, its active fragments, and its active derivatives. Preferably, the polypeptide is a polypeptide having the amino acid sequence of SEQ ID NO: 4 .

The paragraph beginning on page 3, line 13 and ending on page 3, line 22 has been **amended** as follows:

In the present invention, the term "LYC3 polypeptide " or "LYC3 protein " refers to a polypeptide having the activity of LYC3 protein comprising the amino acid sequence of SEQ ID NO: 4 or of ~~positions 20~~amino acids 19-~~148~~146 of SEQ ID NO: 4. The term also comprises the variants of said amino acid sequence which have the same function of human lysozyme. These variants include, but are not limited to, deletions, insertions and/or substitutions of several amino acids (typically 1-50, preferably 1-30, more preferably 1-20, most preferably 1-10), and addition of one or more amino acids (typically less than 20, preferably less than 10, more preferably less than 5) at C-terminal and/or N-terminal. For example, the protein function are usually unchanged when an amino residue is substituted by a similar or analogous one. Further, the addition of one or several amino acids at C-terminal and/or N-terminal will not change the function of protein. The term also includes the active fragments and derivatives of LYC3 protein.

IN THE CLAIMS

Claim 1 has been **amended** as follows:

**1.** (AMENDED) An isolated DNA molecule comprising a nucleotide sequence encoding a polypeptide ~~having human LYC3 protein activity, wherein said nucleotide sequence shares at least 70% homology to~~comprising the ~~nucleotide~~amino acid sequence of ~~nucleotides 81-521 in~~ SEQ ID NO:~~3,~~4 or ~~said nucleotide sequence can hybridize to the nucleotide sequence of nucleotides 81~~amino acids 19-~~521~~146 ~~in~~of SEQ ID NO:~~3 under moderate stringency.~~4.

Claim 3 has been **amended** as follows:

**3.** (AMENDED) The DNA molecule of Claim 1 wherein said nucleotide sequence comprises the nucleotide sequence of nucleotides 81-521 ~~in~~of SEQ ID NO: 3.

Claim 8 has been **amended** as follows:

**8.** (AMENDED) The host cell of claim 7 ~~wherein it comprises~~which is E. coli.

Claim 9 has been **amended** as follows:

**9.** (AMENDED) The host cell of claim 7 ~~wherein it comprises~~which is a eukaryotic cell.

Claim 10 has been **amended** as follows:

**10.** (AMENDED) A method for producing a ~~method for producing a polypeptide having the activity~~LYC3 protein which comprises:

(a) introducing an expression vector for production of LYC3 protein, ~~which comprises the steps of :(a) forming an expression~~said vector ~~of LYC3 protein~~ comprising ~~the~~a

nucleotide sequence encoding ~~the~~a polypeptide having the ~~activity~~amino acid sequence of ~~LYC3 protein,~~SEQ ID NO:4 or of amino acids 20-146 of SEQ ID NO:4, wherein said nucleotide sequence is operably linked ~~with an expression regulatory sequences, and said nucleotide sequence shares~~to at least ~~70% homology to the nucleotide~~one expression control sequence ~~of positions 81-521 in SEQ ID NO: 3;(b) introducing the vector of step (a),~~ into a host cell, thereby forming a recombinant host cell ~~of LYC3 protein~~;

(~~c~~b) culturing the recombinant host cell of ~~step (~~ba) under ~~the~~ conditions suitable for expression of the DNA molecule encoding the polypeptide, such that LYC3 ~~polypeptides~~protein is produced; and

(~~d~~c) isolating the ~~polypeptides having the activity of~~ LYC3 protein so produced.

## Translation products* resulting♦ from each of the three possible reading frames of Jung (v00428)

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Jung Xln1  S R C V Y D T G N M R S L L I L V L C F L P L A A L G K V F G R
Jung Xln2    P A V C T T L A T * G L C * S W C F A S C P W L L W G K S L D D
Jung Xln3      P L C V R H W Q H E V F A N L G A L L P A P G C S G E S L W T
           TCCCGCTGTGTGTACGACACTGGCAACATGAGGTCTTTGCTAATCTTGGTGCTTTGCTTCCTGCCCCTGGCTGCTCTGGGGAAAGTCTTTGGACGA

Jung Xln1  C E L A A A M K R H G L D N Y R G Y S L G N W V C V A K F E S N
Jung Xln2    V S W Q R L * S V T D L I T I G D T A W E T G C V L Q N S R V T
Jung Xln3  M * A G S G Y E A S R T * * L S G I Q P G K L G V C C K I R E *
           TGTGAGCTGGCAGCGGCTATGAAGCGTCACGGACTTGATAACTATCGGGGATACAGCCTGGGAAACTGGGTGTGTGTTGCAAAATTCGAGAGTAAC

Jung Xln1  F N T Q A T N R N T L D G S I D Y G L L Q I N S R W W C N D G R T
Jung Xln2    S T P R L Q T V T P M G V P T T E S Y R S T A A G G A T M A G P
Jung Xln3  L Q H P G Y K P * H R W E Y R L R N P T D Q Q P L V V Q R W Q D
           TTCAACACCCAGGCTACAAACCGTAACACCGATGGGAGTACCGACTACGGAATCCTACAGATCAACAGCCGCTGGTGGTGCAACGATGGCAGGACC

Jung Xln1  P G S R N L G N I P G S A L L S S D I T A S V N C A K K I V S D
Jung Xln2    Q A P G T C A T S R A Q P C * A Q T * Q R A * T A R R R S S A M
Jung Xln3  P R L Q E P V Q H P V L S P A E L R H N S E R E L R E E D R Q R
           CCAGGCTCCAGGAACCTGTGCAACATCCCGTGCTCAGCCCTGCTGAGCTCAGACATAACAGCGAGCGTGAACTGCGCGAAGAAGATCGTCAGCGAT

Jung Xln1  G N C M S A W V A W R N R C K G T D V Q A W I R G C R L * G A A
Jung Xln2    E T A * A R G S P G A T A A R V P T S R R G S E A A G C E E L P
Jung Xln3  W K R H E R V G R L A Q P L Q G Y R R P G V D Q R L P A V R S C
           GGAAACGGCATGAGCGCGTGGGTCGCCTGGCGCAACCGCTGCAAGGGTACCGACGTCCAGGCGTGGATCAGAGGCTGCCGGCTGTGAGGAGCTGCC

Jung Xln1  A P G P P A A Q P A A L R A R R Y P L G S F K R I P H * N D Y T Q T
Jung Xln2    H P A R P L H S R P L C E R D A T R L A V L N A S L I K T T I R K R
Jung Xln3  R T R P A R C T A G R F A S A T L P A W Q F * T H P S L K R L Y A N A
           GCACCCGGCCCGCCCGCTGCACAGCCGGCCGCTTTGCGAGCGCGACGCTACCCGCTTGGCAGTTTTAAACGCATCCCTCATTAAAACGACTATACGCAAACGCC
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* Translation product taught by Jung is highlighted.

♦ Translated using Vector NTI available from Informax at http://www.informaxinc.com/.

## These translation products were aligned** with Yu et al.'s SEQ ID NO:4 using ClustalW†‡:

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                1               15 16              30 31              45 46              60 61              75
Yu SEQ ID#4 ---------MLLALV CLLSCLLPSSEAKIY GRCELARVLHDFGLD GYRGYSLADWV--CL AYFTSGFNAAAALDYE    64
Jung Xln1   SRCVYDTGNVRSLII LVLCFLPLAALCKVF GRCELAAAMKRHGLD NYRGYSLGNWV--CV AKFESNFNTQATNRN    73   (29/64)
Jung Xln2   ------PAVCTTLAT GLCSWCFASCPWLLW GKSLDDVSWQRLSVT DLITIGDTAWETGCV LQNSRVTSTPRLQTV    69   ( 8/64)
Jung Xln3   ----PLCVRHWQHEV FANLGALLPAPGCSG ESLWTMAGSGYEASR TLSGIQPGKLGVCCK IRELQHPGYKPHRWF    71   ( 5/64)

                76              90 91              105 106             120 121             135 136             150
Yu SEQ ID#4 ADGSTNNGIFQINSR RWCSN--LITPNVPNV CRMYCSDLLNPNLKD IVICAMKITQFPQGL GYWEAWRHHCQGKDL   137
Jung Xln1   TDGSTDYGILQINSR WWCNDG-RTPGSRNL CNIPCSALLSSDITA SVNCAKKIVSDGNGM SAWVAWRNRCKGTDV   147   (34/73)
Jung Xln2   TPMGVPTTESYRSTA AGGATM-AGPQAPGT CATSRAQPCAQTQRA LAR-RRSSAMETAAR GSPGATAARVPTSRR   142   ( 7/73)
Jung Xln3   YRLRNPTDQQPLVVQ RWQDPRLQEPVQHPV LSPAELRHNSERELR EEDRQRWKRHERVGR LAQPLQGYRRPGVDQ   146   ( 8/73)

                151             165 166             180 181             195 196         210
Yu SEQ ID#4 -TEWVDGGDF----- --------------- --------------- -     146
Jung Xln1   -QAWIRGGRLGAAAP GPPAAQPAALRARRY PLGSFKRIPHNDYTQ T     192   (3/9)
Jung Xln2   -GSEAAGGEELPHPA RPLHSRPLCERDATR LAVLNASLIKTTIRK R     187   (2/9)
Jung Xln3   RLPAVRSGRTRPARC TAGRFASATLPAWQF THPSLKRLYANA--- -     188   (2/9)
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Jung Xln1 → 66/146 = 45.2%
Jung Xln2 → 17/146 = 11.6%
Jung Xln3 → 15/146 = 10.3%

** Residues that match Yu SEQ ID#4 are highlighted.

† Default settings.

‡ Available at http://dot.imgen.bcm.tmc.edu:9331/multi-align/Options/clustalw.html.